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BOZICEVIC, FIELD & FRANCIS LLP  
1900 UNIVERSITY AVENUE  
SUITE 200  
EAST PALO ALTO, CA 94303

EXAMINER
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CROW, ROBERT THOMAS

ART UNIT	PAPER NUMBER
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1634

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/810,333

Applicant(s)

HEEGER ET AL.

Examiner

Robert T. Crow

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,7,8,12-16,25,28-34,39,40,47,48,55,56 and 59-62 is/are pending in the application.
- 4a) Of the above claim(s) 39,40,47,48,55,56 and 59-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7,8,12-16,25 and 28-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/07, 1/08, 11/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Status of the Claims*

1. This action is in response to papers filed 20 November 2007 in which claims 1, 7, 12-13, and 25 were amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The interview summary filed 2 January 2008 is acknowledged and the interview record is complete.

The previous rejections under 35 U.S.C. 112, first paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1, 7-8, 12-16, 25, and 28-34 are under prosecution.

2. This action is non-final because while the previous Office Actions filed 21 August 2006 and 3 April 2007 rejected all of the claims, Section 9 of the previous Office Action filed 15 August 2007 did not include the previously presented rejection of claim 29. In addition, while Section 9 of the Office Action filed 15 August 2007 included rejections for claims 1, 7-8, 12, 14-16, 25, 28, and 30-34, the first paragraph of Section 9 did not list claims 25, 28, and 30-34 as rejected.

### *Terminal Disclaimer*

3. The terminal disclaimer filed on 20 November 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of Applicant No.

11/193,318 has been reviewed and was accepted on 7 December 2007. The previous rejections under the judicially created doctrine of obviousness-type double patenting are therefore withdrawn.

*Information Disclosure Statement*

4. The Information Disclosure Statements filed 13 December 2007 and 18 January 2008 are acknowledged. However, the first page of the Information Disclosure Statement of 13 December 2007 is crossed out because no references are listed on the page.

In addition, U.S. Patent Nos. 5,312,728 and 6,264,825 are lined through on the Information Disclosure Statement of 18 January 2008 because they were previously cited in the PTO Form 892 filed 21 August 2006. U.S. Patent No. 6,221,586 is lined through because it was previously cited in the Information Disclosure Statement of 15 January 2007.

The Information Disclosure Statement of 18 November 2004 is included with this Office Action because U.S. Patent No. 5,139,812 was not initialed previously. The remaining references are lined through and crossed out to avoid duplication on the record.

*Specification*

5. The use of trademarks (e.g., Lipitor and Neupogen) has been noted in this application. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

*Claim Rejections - 35 USC § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 7-8, 12, 14-16, 25, and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825 B1, issued 24 July 2001) in view of Lizardi et al (U.S. Patent No. 5,312,728, issued 17 May 1994).

Regarding claims 1 and 12, Blackburn et al teach a detector. In a single exemplary embodiment, Blackburn et al teach a detector comprising an electrode capable of sensing redox events in a redox moiety in the form of a detection electrode for detecting electron transfer (column 2, lines 14-24). A probe is immobilized on the detection electrode (column 13, lines 10-13). The "capture binding ligands" of Blackburn et al are interpreted as probes because they are capture probe nucleic acids (column 40, lines 29-40), and they allow the attachment of the target analyte to the detection electrode for the purposes of detection (column 39, lines 12-65). The probe of Blackburn et al comprises a redox moiety in the form of

an ETM (column 66, lines 9-44) wherein an ETM is an electron transfer moiety (i.e., redox moiety; Abstract).

Blackburn et al further teach the probe is an oligonucleotide having a hairpin stem-loop structure comprising the redox moieties 135 at an end of the probe (column 66, lines 9-44 and Figure 12), wherein either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Thus, Blackburn et al teach an embodiment wherein in the absence of the specific interaction of hybridization between the target nucleic acid with the probe, redox moiety 135 is in a first position. Upon binding to the target, the hairpin stem loop structure is altered, which moves the redox moiety to a second position. The first and second positions give rise to distinguishable redox events detectable by the electrode because detection of the binding proceeds through the use of the ETM redox moieties (Abstract).

Blackburn et al also teach either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Therefore, one terminus of the probe is immobilized and the redox moiety 135 at the other terminus.

Blackburn et al do not teach the end of the probe bearing the redox moiety moves closer to the electrode upon binding the target; i.e., wherein the second position is closer to the electrode than the first position, thereby providing more efficient electron transfer to the electrode (i.e., claim 1), or wherein the second position arises from a configuration comprising internal hybridization between two regions of the probe (i.e., claim 12).

However, Lizardi et al teach a single switch probe nucleic acid molecule having two alternate conformations in the presence and absence of a target molecule 8 (column 14, Example V and Figures 12-15). Figure 12 illustrates the probe 30 in the absence of an oligonucleotide target, and Figure 13 shows the alternate conformation of the probe in the presence of the target 8 (column 14, Example V). Figure 13 further shows internal hybridization between two regions of the probe because hairpin 36 is formed after binding to the target (i.e., claim 12). Lizardi et al also teaches the probes have the added advantage of

allowing exponential replication of the target polynucleotide (column 14, lines 40-41), which generates up to a billion copies of a single target molecule in a single step (column 3, lines 48-50). Thus, Lizardi et al teach the known technique wherein the configuration of a probe changes such that one end moves closer to the other end upon binding to a target.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the detector comprising a probe having one terminus immobilized and the other terminus labeled with a redox moiety as taught by Blackburn et al with the switch probe of Lizardi et al with a reasonable expectation of success. The modification would result in the probe of Lizardi et al being immobilized at end 35 as shown in Figure 12 of Lizardi et al and the redox moiety at end 32 in accordance with the immobilization and labeling taught by Blackburn et al. Upon binding, end 32 would move closer to end 35, as depicted in Figure 13, thereby promoting electron transduction to the electrode because the redox moiety is now closer to the electrode, in accordance with the embodiment described in Figure 3 and paragraph 0045 of the instant specification. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding "promoting electron transduction" (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1])). The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a detector having the added advantage of having probes that allow production of a billion copies of a potentially scarce target in a single step amplification of as explicitly taught by Lizardi et al (column 3, lines 48-50). In addition, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Lizardi et al could have been applied to the detector of Blackburn et al with predictable results because the probe configuration of Lizardi predictably results in probes useful for detection of target nucleic acids.

Regarding claim 7, the detector of claim 1 is discussed above. Blackburn et al further teach the probe is immobilized on the electrode on a position distant from the redox moiety because either the 3' or

5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25) and the redox moiety 135 at the other terminus (Figure 12)

Regarding claim 8, the detector of claim 1 is discussed above. Blackburn et al further teach the electrode is capable of inducing redox events in the redox moiety; namely, the detector comprises an amperometric device for applying a potential to the electrode and different currents result because of electron transfer (column 82, lines 7-20).

Regarding claims 14-15, the detector of claim 1 is discussed above. Blackburn et al further teach the electrode comprises a metal; namely, gold (column 2, lines 60-65).

Regarding claim 16, the detector of claim 1 is discussed above. Blackburn et al further teach the redox moiety is ethidium bromide (column 49, lines 15-40).

Regarding claim 25, Blackburn et al teach a detector. In a single exemplary embodiment, Blackburn et al teach a detector comprising an electrode capable of sensing redox events in a redox moiety in the form of a detection electrode for detecting electron transfer (column 2, lines 14-24). A probe is immobilized on the detection electrode (column 13, lines 10-13). The "capture binding ligands" of Blackburn et al are interpreted as probes because they are capture probe nucleic acids (column 40, lines 29-40), and they allow the attachment of the target analyte to the detection electrode for the purposes of detection (column 39, lines 12-65). The probe of Blackburn et al comprises a redox moiety in the form of an ETM (column 66, lines 9-44) wherein an ETM is an electron transfer moiety (i.e., redox moiety; Abstract).

Blackburn et al further teach the probe is an oligonucleotide having a hairpin stem-loop structure comprising the redox moieties 135 at an end of the probe (column 66, lines 9-44 and Figure 12), wherein either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Thus, Blackburn et al teach an embodiment wherein in the absence of the specific interaction of hybridization between the target and the probe, redox moiety 135 is in a first position. Upon binding to the target, the hairpin stem loop structure is altered, which moves the



redox moiety to a second position. The first and second positions give rise to distinguishable redox events detectable by the electrode because detection of the binding proceeds through the use of the ETM redox moieties (Abstract).

Blackburn et al also teach either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Therefore, one terminus of the probe is the instantly claimed first region that is immobilized to the electrode and the redox moiety 135 at the other terminus, which is the instantly claimed third region. The intermediate nucleotides are the second region, which form a first loop by hybridization of first and second nucleotide sequences within the second region (e.g., Figure 12).

Blackburn et al do not teach the end of the probe bearing the redox moiety moves closer to the electrode upon binding the target; i.e., wherein the second position is closer to the electrode than the first position, thereby providing more efficient electron transfer to the electrode, or wherein the second region forms a second hybridization loop upon binding the target between two regions of the probe.

However, Lizardi et al teach a probe nucleic acid that is a single molecule (e.g., column 14, Example V and Figures 12-13). Figure 12 illustrates the probe 30 in the absence of an oligonucleotide target, and Figure 13 shows the alternate conformation of the probe in the presence of the target (column 14, Example V). Lizardi et al teach the probe has switch sequences, which hybridize to each other in the absence of a target (column 5, lines 45-50). Figure 12 comprises element 32, wherein the terminus at 32 is the third region. Lizardi et al also teach switch sequences and probe sequences overlap (column 7, lines 47-55); thus, the second region of the instantly claimed probe comprises the remainder of element 32 as well as elements 33 and 34. The second region self hybridizes to form first loop 31 and a stem between part of 32 and 33, which are the first and second nucleotide sequences. The third region of the probe is element 35, which is located at the other end of the probe.

Figure 13 shows that upon hybridization to oligonucleotide target 8, loop 31, which is the probe sequence, is hybridized to the target. Because Lizardi et al teach switch sequences and probe sequences

overlap (column 7, lines 47-55), part of 32, which is the first nucleotide sequence of the second region, also hybridizes to the target. The remaining part of 32, which is in the second region, hybridizes to part of 34, which is also part of the second region, thereby forming self-hybridized second loops 33 and 36 in the detectable ribozyme structure of Figure 13 (column 14, Example V). Lizardi et al also teaches the probes have the added advantage of allowing exponential replication of the target polynucleotide (column 14, lines 40-41), which generates up to a billion copies of a single target molecule in a single step (column 3, lines 48-50). Thus, Lizardi et al teach the known technique of using a probe having the structural limitations of the instant claim.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the detector comprising a probe having one terminus immobilized and the other terminus labeled with a redox moiety as taught by Blackburn et al with the switch probe of Lizardi et al with a reasonable expectation of success. The modification would result in the probe of Lizardi et al being immobilized at end 35 as shown in Figure 12 of Lizardi et al and the redox moiety at end 32 in accordance with the immobilization and labeling taught by Blackburn et al. Upon binding, end 32 would move closer to end 35, as depicted in Figure 13, thereby promoting electron transduction to the electrode because the redox moiety is now closer to the electrode, in accordance with the embodiment described in Figure 3 and paragraph 0045 of the instant specification. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding "promoting electron transduction." The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a detector having the added advantage of having probes that allow production of a billion copies of a potentially scarce target in a single step amplification of as explicitly taught by Lizardi et al (column 3, lines 48-50). In addition, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Lizardi et al could have been applied to the detector of Blackburn et al with predictable

results because the probe configuration of Lizardi predictably results in probes useful for detection of target nucleic acids.

Regarding claim 28, the detector of claim 25 is discussed above. Blackburn et al further teach the detector comprises a detector for detecting electron transduction between the electrode and the redox moiety when the second loop is formed; namely, an AC detector (column 83, lines 55-65).

Regarding claim 29, the detector of claim 28 is discussed above. Blackburn et al also teach an indicator for inducing electron transduction; namely, an amperometric device for applying a potential to the electrode, wherein different currents result because of electron transfer (column 82, lines 7-20).

Regarding claims 30-31, the detector of claim 29 is discussed above. Blackburn et al further teach the first region is at one end of the probe and the third region is at the second end of the probe because either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25) and the redox moiety 135 at the other terminus (Figure 12)

Regarding claims 32-33, the detector of claim 25 is discussed above. Blackburn et al further teach the electrode comprises a metal; namely, gold (column 2, lines 60-65).

Regarding claim 34, the detector of claim 33 is discussed above. Blackburn et al further teach the redox moiety is ethidium bromide (column 49, lines 15-40).

9. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825 B1, issued 24 July 2001) in view of Lizardi et al (U.S. Patent No. 5,312,728, issued 17 May 1994) as applied to claim 1 above, and further in view of Rothberg et al (U.S. Patent Application Publication No. US 2002/0012930 A1, published 31 January 2002).

Regarding claim 13, the detector of claim 1 is discussed above in Section 8.

Neither Blackburn et al nor Lizardi et al teach loops in the target and the probe in the second position (i.e., during hybridization).

However, Rothberg et al teach probes hybridized to targets wherein the probe and the target have a loop during hybridization; namely, Figure 1D, wherein the hybridized probe leaves a loop in the probe and target in the form of the gapped region and a loop in the form of the single stranded portion of the rolling circle template molecule (Figure 1D). Rothberg et al teach the loop in the target has the added advantage of allowing detection of single nucleotide polymorphisms in the gap (paragraph 0091). Single nucleotide polymorphisms are indicative of genetic diseases. Thus, Rothberg et al teach the known technique of using a probe having loops after hybridization to a target.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the detector as taught by Blackburn et al in view of Lizardi et al with the loop regions in the target and the probe as taught by Rothberg et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a detector having the added advantage of allowing detection of markers of genetic disease as a result of detection of single nucleotide polymorphisms in the gap as explicitly taught by Rothberg et al (paragraph 0091). In addition, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Rothberg et al could have been applied to the detector of Blackburn et al in view of Lizardi et al with predictable results because the probe configuration of Rothberg et al predictably results in probes useful for detection of target nucleic acids.

#### *Response to Arguments*

10. Applicant's arguments filed 20 November 2007 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on page 14 of the Remarks that Blackburn et al does not teach a probe that is both immobilized on an electrode and comprises a redox moiety because column 13, lines 10-13 merely refers to electrophoresis electrodes, not detection electrodes.

However, column 13, lines 10-13 explicitly teach "capture binding ligands immobilized on the detection electrodes" which bind to the target. The capture binding ligands are interpreted as probes because they are capture probe nucleic acids (column 40, lines 29-40), and they allow the attachment of the target analyte to the detection electrode for the purposes of detection (column 39, lines 12-65). Thus, column 13, lines 10-13 does teach the probes are bound to the detection electrodes.

B. Applicant further argues on pages 14-15 of the Remarks that Blackburn et al does not teach a probe that is both immobilized on an electrode and comprises a redox moiety because column 41, lines 17-25 teaches conductive oligomers rather than probes per se, and does not teach a redox moiety on the conductive oligomer.

However, column 41, lines 17-25 explicitly teaches the "capture probe nucleic acid is covalently attached to the electrode via a conductive oligomer." The conductive oligomer is interpreted as part of the electrode; thus, the probe is attached to the electrode.

Further, as detailed above in the rejection, Blackburn et al teach the probe is an oligonucleotide having a hairpin stem-loop structure with the redox moieties 135 at an end of the probe (column 66, lines 9-44 and Figure 12); thus, the conductive oligomer is not relied upon for the redox moiety because the redox moiety is on the probe.

C. Applicant asserts on pages 14-15 of the Remarks that column 66, lines 9-44 refers only to amplifier probes and not the capture probes.

However, column 66, lines 9-44 of Blackburn et al specifically teaches "the amplifier probes, or any of the other probes of the invention, may form hairpin stem-loop structures in the absence of their target (emphasis added by examiner)." Thus, Blackburn et al teach the hairpin probes are the detection probes.

D. In response to applicant's argument on page 14 of the Remarks that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

E. Applicant argues on page 15 of the Remarks that none of the molecules of Lizardi et al include a redox moiety or are bound to an electrode.

However, the teachings of Lizardi et al are not relied upon for either redox moieties or immobilization on electrodes; rather, Lizardi et al are merely relied upon for probe conformations that move one end of the probe closer to the other end of the probe after hybridization to a target molecule.

F. Applicant argues on page 16 of the Remarks that the proposed combination of Blackburn et al with Lizardi is fatally flawed because neither reference teaches a probe bound directly to an electrode and includes a redox moiety.

However, as noted above, Blackburn et al teach the "capture probe nucleic acid is covalently attached to the electrode via a conductive oligomer." The conductive oligomer is interpreted as part of the electrode; thus, the probe is attached to the electrode. Further, as detailed above in the rejection, Blackburn et al teach the probe is an oligonucleotide having a hairpin stem-loop structure with the redox moieties 135 at an end of the probe (column 66, lines 9-44 and Figure 12).

G. Applicant further argues on pages 16-17 of the Remarks that the practicing the invention in a manner providing the suggested modification renders the invention useless because Lizardi et al suggests in columns 3 and 4 that the probes of Figures 12 and 13 result in non-specific binding.

However, neither of columns 3-4 refer to the probes of the cited figures. In addition, columns 3-4 are clearly background material that precedes the "Summary of the Invention" in column 5 and the "Description of the Drawings and "Detailed Description of the Invention" starting in column 6, both of which detail the probes of Figures 12-13.

H. Applicant's further arguments on page 17 of the Remarks refer to cleavage of the probe such that redox reactions are no longer detectable.

However, Applicant is merely arguing a hypothetical use of the probe not required in the rejection, rather than the structural limitations of the probe for which Lizardi et al is relied upon. The ordinary artisan would clearly recognize that following detection of the redox reaction as taught by Blackburn et al, amplification based on the probes of Lizardi et al is subsequently performed to afford the additional copies of a potentially scarce target in a single step amplification procedure as taught by Lizardi et al.

In addition, it is also noted that under the Supreme Court ruling for *KSR Int'l Co. v. Teleflex, Inc* (No 04-1350 (US 30 April 2007) forecloses the argument that a specific teaching suggestion, or motivation is required to support a finding of obviousness. See *Ex parte Smith* (USPQ2d, slip op. at 20 (Bd. Pat. App. & Interf. June 25, 2007). Thus, as noted above, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Lizardi et al could have been applied to the detector of Blackburn et al with predictable results because the probe configuration of Lizardi predictably results in probes useful for detection of target nucleic acids.

I. Applicant's arguments on pages 17-18 of the Remarks regarding claim 13 rely on arguments set forth to address the rejections of the claims as obvious over Blackburn et al in view of Lizardi et al under 35 USC 103(a). These arguments are addressed above. Since the arguments regarding the teachings of Blackburn et al in view of Lizardi et al were not persuasive, the rejection of the claim 13 is maintained.

*Conclusion*

11. No claim is allowed.
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow  
Examiner  
Art Unit 1634



DIANA JOHANNSEN  
PRIMARY EXAMINER